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Reflux Following Esophagectomy for Esophageal Cancer

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Gastroesophageal reflux is a common problem after gastroesophageal resection and reconstruction, despite the routine prescription of proton pump inhibitors (PPIs). Resection of the lower esophageal sphincter and excision of the vagus nerve are generally thought to be the main factors that interfere with gastric motor function. However, physiological studies of reflux symptoms after esophagectomy are still lacking. Gastroesophageal reflux occurs frequently after esophagectomy, but there is no known effective method to prevent it. Therefore, in order to manage gastroesophageal reflux after esophagectomy, strict lifestyle modifications and gastric acid suppression treatment such as PPIs are needed, and further clinical studies are required.

Keywords: Esophageal neoplasms, Gastroesophageal reflux, Esophagectomy

Introduction

Esophageal cancer is one of the most difficult diseases to cure. Surgery is the main treatment modality for patients with resectable esophageal cancer [1,2]. In our clinical practice, we have found that many patients experience several episodes of intolerable gastrointestinal side effects after esophagectomy. Conventional surgical procedures result in poor postoperative quality of life (QOL) [3-5]. However, information on the function and QOL of long-term survivors after esophageal resection for carcinoma is limited. Recently developed minimally invasive surgical treatments for esophageal cancer, such as robotic/thoracoscopic/laparoscopic surgery and perioperative management, may improve postoperative QOL. The common symptoms after esophagectomy are dysphagia, reflux, delayed gastric emptying, and eating problems. The functional symptoms identified were reflux (39%), delayed gastric emptying (37%), dumping (21.4%), and anastomotic stenosis (16%) [6].

Among several factors influencing QOL, reflux after esophagectomy is a troublesome complication regarding QOL. Reflux disease is considered to be an unavoidable consequence of esophageal resection following gastric interposition [7,8].

Although reflux after esophagectomy appears to be an inevitable complication after surgery for esophageal cancer, we have tried to find out how to prevent or overcome it based on a detailed review of the literature.

The basic pathophysiology of reflux after esophagectomy

Generally, gastric acid reflux is a symptom that occurs when the stomach is located within the chest cavity after esophagectomy. When lying down or sleeping, the position or posture is the main cause of worsening symptoms. Clinically, reflux manifests as regurgitation that causes the symptom of heartburn. Coughing, postprandial pain, and belching are other atypical symptoms of reflux after esophagectomy.

The disruption of normal anti-reflux mechanisms including the lower esophageal sphincter, angle of His, and diaphragmatic muscle and the denervation of the vagus nerve are generally thought to be the main factors that interfere with gastric motor function. However, physiological

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studies of reflux symptoms after esophagectomy are still lacking. Furthermore, the pressure difference between thoracic (negative) and abdominal cavity (positive) is another factor that promotes reflux across the anastomosis.

By definition, reflux is clinically suspected in patients who experience burning discomfort, localized behind the breastbone with or without extraesophageal symptoms (cough, asthma, discomfort of the pharyngolarnyx, etc.). Esophageal pH monitoring is an objective method used to evaluate reflux after esophagectomy. Yuasa et al. [9] reported elevated acid reflux (28%) and elevated duodenogastroesophageal reflux (44%) in esophagectomy patients. They revealed that both gastroesophageal reflux (GER) and duodenogastroesophageal reflux were more common in the supine position than in other positions [9]. Another report showed that 71.6% of esophagectomy patients had reflux esophagitis [10]. Generally, catheters have been used for 24-hour impedance-pH monitoring. The esophageal pH sensor is placed 1.5 cm distal to the upper esophageal sphincter and the gastric pH sensor is located 15 cm distal to the esophageal pH sensor for pH monitoring. Using this method, Kim et al. [11] showed that GER was frequent in patients following esophagectomy, but GER did not increase the risk of anastomosis site stricture and aspiration pneumonia in a study of patients who took proton pump inhibitors (PPIs) after esophagectomy and were instructed to sleep in a supine position with the head of the bed at approximately 30° to 45°.

Furthermore, several different surgical options exist, including whether to perform a pyloric drainage procedure (no drainage or pyloroplasty), the surgical method (open, video-assisted thoracoscopic surgery [VATS], or robot-assisted thoracoscopic surgery [RATS]), the approach (3-hole, Ivor Lewis, or transhiatal), the conduit (stomach, colon, or jejunum), and the route (subcutaneous, substernal, or post-mediastinal). For example, a minimally invasive approach (VATS or RATS) has some possible limitations regarding the length of the gastric tube, which might make the height of the anastomosis level lower than when the open approach is used. These variations result in different clinical outcomes regarding reflux after esophagectomy.

The following factors influence reflux after esophagectomy

Pyloric drainage procedures

Pyloric drainage procedures may facilitate gastric emptying and reduce reflux. However, they may promote duodenal reflux and bile reflux into the esophagus.

A study reported a significant reduction in regurgitation and reflux symptoms in patients in whom a drainage procedure had been performed, compared with those who had not received a drainage procedure [12]. In another randomized controlled study, the researchers showed that pyloroplasty made no difference regarding the symptoms of reflux or the mean concentration of bile in gastric fluid at 6 months after esophagectomy and intrathoracic anastomosis [13].

Truncal vagotomy also decreases gastric emptying and impairs gallbladder function, which are processes that are thought to increase gastric exposure to bile. Gutschow et al. [14] reported that gastric exposure to bile after truncal vagotomy and transposition of the stomach up to the neck was pathologic in three-quarters of patients. Both the supine position and a history of a gastric drainage procedure are suspected to the promote reflux of duodenal juices into the denervated intrathoracic stomach.

Level of the anastomosis

Anastomoses made below the level of the aortic arch are considered to predispose individuals to reflux symptom. The theoretical basis for this that a lower location of the anastomosis site means that more of the stomach is located in the abdominal cavity, which is a positive-pressure environment.

Shibuya et al. [10] retrospectively compared the rate of reflux esophagitis between patients with a neck anastomosis (56.4%) and patients with an intrathoracic anastomosis (88.6%). They found a significantly lower incidence of reflux esophagitis in patients with a neck anastomosis [10]. Wormald et al. [15] reported a reflux rate of 30.6% and a dysphagia rate of 14.4% in their patients who received cervical anastomoses. Of course, additional clinical studies continue to be needed to reach a more solid conclusion regarding the relationship of GER with the anastomosis height, as this relationship is still a matter of dispute [16].

Route of the conduit

Inconsistent results have been reported on whether the use of the posterior mediastinal pathway rather than other routes affects reflux after esophagectomy. The route of the esophageal conduit may also affect GER due to the angulation and length problem of the anastomotic area. Tsubuku et al. [17] showed that gastric acidity, as assessed by the percentage (%) of time with a pH <4, was reduced after

esophagectomy, and the posterior mediastinal route had higher percentages of time with acidic conditions than the retrosternal or subcutaneous routes. However, only 40 patients were enrolled in their study, and the interpretation was limited due to the small number of patient groups for each route (posterior mediastinal route, n=17; retrosternal route, n=10; subcutaneous route, n=13). Further studies are needed to understand the relationship between the route of the esophageal conduit and GER.

Gastric tube versus whole stomach

Currently, both the gastric-tube and whole-stomach approaches are widely used for esophagogastric anastomoses [18,19]. Some studies have concluded that the whole-stomach approach is superior to the gastric-tube approach [20,21]. In contrast, other studies have shown that the anatomical structure of the gastric tube is more in line with physiological needs, which could reduce the incidence of postoperative complications [22].

However, the meta-analysis of Zhang et al. [23] found that the incidence of reflux esophagitis was lower in patients who underwent gastric tube reconstruction than in patients who underwent reconstruction with the whole stomach. This meta-analysis study investigated 6 studies to obtain the most comprehensive evidence regarding this issues. The following reasons might explain their findings: (1) the shape of the stomach tube can shorten the retention time of food in the stomach, which decreases the incidence of reflux; (2) the oxyntic glands in the stomach, which are composed of parietal cells, chief cells, and mucous neck cells, are mainly distributed in the gastric corpus and gastric fundus; and (3) the volume of the tubular stomach is smaller than that of the whole stomach [23-26].

However, controversy remains regarding which gastric conduit method (whole stomach versus gastric tube) is more reasonable after esophagectomy in terms of reflux esophagitis.

Anti-reflux surgery following esophagectomy

First of all, anti-reflux surgery following esophagectomy is rarely used in the current era. The majority of anti-reflux surgical procedures are experimental, and insufficient information has been gathered to support their clinical utility.

Nonetheless, a number of surgical methods have been developed to control reflux after esophagectomy: (1) intercostal muscle flaps as anti-reflux valve [27,28]; (2) valvuloplastic esophagogastrostomy [29-31]; (3) inkwell esophagogastrostomy [32,33]; and (4) globe-type anti-reflux surgery [34-36]. Various other types of anti-reflux surgery are also being performed, but as mentioned earlier, they have not been widely used, and more clinical studies are needed.

Proton pump inhibitors after esophagectomy

In general, PPIs are recommended to prevent reflux esophagitis and anastomotic stricture [37]. The symptoms of reflux are variable and have a very complex etiology. While typical symptoms have been found to respond relatively well to PPIs, that is not the case for atypical symptoms such as respiratory symptoms [38]. Okuyama et al. [39] revealed that PPIs effectively suppress gastric acid production, thereby relieving reflux-related symptoms and perhaps reducing the risk of esophagogastric anastomotic stricture. Most thoracic surgeons use PPIs to prevent anastomotic stricture, but the effect of PPIs on reflux prevention has not yet been determined.

Conclusion

Reflux frequently occurs after esophagectomy because normal anti-reflux mechanisms have been compromised. The general strategy for reflux esophagitis after esophagectomy is lifestyle modification and PPI use. Several factors are related with reflux after esophagectomy (e.g., gastric conduit, route, and pylorus procedure), but conclusive evidence does not yet exist for specific options.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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